L Number	Hits	Search Text	DB	Time stamp
1	96076	ataxia-telangiectasia or ataxia adj telengiectasia or ATM	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/07/30 09:42
2	564	ataxia-telangiectasia or ataxia adj telengiectasia	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/07/30 09:43
3	91	(ataxia-telangiectasia or ataxia adj telengiectasia) and ATM	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/07/30 10:11
4	22	(ataxia-telangiectasia or ataxia adj telengiectasia) and ATM same (deficient or deleted) same cell	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/07/30 09:46
5	5	ATM adj (deficient or deleted) adj cell	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/07/30 10:29
6	10	ATM adj (deficient or deleted) same cell	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/07/30 09:58
8	460	(ataxia-telangiectasia or ataxia adj telengiectasia) and virus	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/07/30 09:59
9	10	(ATM adj (deficient or deleted) same cell) and virus	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/07/30 09:59
10	289	ATM same (cloning or clone or subclone or vector)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/07/30 10:13
11	20	(ATM same (cloning or clone or subclone or vector)) and vaccinia	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/07/30 10:29
12	52	Mec1	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/07/30 10:24
13	25	Mec1 and ATM	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/07/30 10:24
14	63	ATM and (deficient or deleted) adj cell	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/07/30 10:32

15	13	(ATM and (deficient or deleted) adj cell) and vaccinia	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/07/30 10:25
16	4	Mecl and (deficient or deleted) adj cell	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/07/30 10:37
17	3	(Mecl and (deficient or deleted) adj cell) and atm	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/07/30 10:37
-	358	ataxia-telangiectasia	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/07/30 09:41
-	147999	(viral or virus) same mammalian	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/11 15:22
-	215	ataxia-telangiectasia and ((viral or virus) same mammalian)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/11 15:22
-	214	(ataxia-telangiectasia and ((viral or virus) same mammalian)) and expression	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/11 15:23
-	1	(ataxia-telangiectasia and ((viral or virus) same mammalian)) and expresion	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/11 15:23
-	44	ataxia-telangiectasia same expression	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/11 15:25
-	3	(ataxia-telangiectasia same expression) and ((viral or virus) same mammalian)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/11 15:23
-	61	ataxia-telangiectasia same protein	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/11 15:25
-	45	(ataxia-telangiectasia same protein) and (virus or adenovirus or viral adj vector)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/11 15:33
-	8	ataxia-telangiectasia same (virus or adenovirus or viral adj vector)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/11 15:27
-	48	ataxia-telangiectasia same (expression or production)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/11 15:27

-	2075558	ataxia-telangiectasia adj10\ (expression or production)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/11 15:29
-	0	ataxia-telangiectasia adj10 (expression or production)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/11 15:29
-	2	ataxia-telangiectasia adj20 (expression or production)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/11 15:29
-	4	(ataxia-telangiectasia same protein) same (virus or adenovirus or viral adj vector)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/11 15:34
-	102	ataxia-telangiectasia same polypeptide	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/11 16:09
-	90	(ataxia-telangiectasia same polypeptide) and production	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/11 16:09
-	0	((ataxia-telangiectasia same polypeptide) and production) and Barlow	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/11 16:10
-	31	"0112647"	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/11 16:10
-	0	"0112647" and barlow	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/11 16:10
-	8637	Barlow, Carolee	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/11 16:10
-	8838	Callahan	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/11 16:11
-	8	Callahan and Barlow	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/11 16:11
-	206	ataxia-telangiectasia and vaccinia	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/18 12:21
-	262911	method adj2 producing	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/18 12:17

-	139	(method adj2 producing) same vaccinia	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/18 12:19
-	0	((method adj2 producing) same vaccinia) and ((ataxia-telangiectasia and vaccinia)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/18 12:19
-	188	(method adj2 producing) and (ataxia-telangiectasia and vaccinia)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/18 12:19
-	188	((method adj2 producing) and (ataxia-telangiectasia and vaccinia)) and virus	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/18 12:19
-	0	ataxia-telangiectasia same (method adj2 producing)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/18 12:21
-	0	(method adj2 producing) same vaciinia	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/18 12:16
-	138	(method adj2 producing) same vaccinia	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/18 12:17
-	240728	method adj1 producing	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/18 12:18
-	137	(method adj1 producing) same vaccinia	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/18 12:21
-	16	(method adj1 producing) adj10 vaccinia	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/19 17:51
-	147	(method adj1 producing) same (vaccinia or poxvirus)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/18 12:21
-	0	ataxia-telangiectasia and ((method adj1 producing) same (vaccinia or poxvirus))	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/18 12:21
-	0	ataxia-telangiectasia same (method adj2 producing)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/18 12:22
-	209	ataxia-telangiectasia and (method adj2 producing)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/18 12:22

-	188	(ataxia-telangiectasia and (method adj2 producing)) and (vaccinia or poxvirus)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/18 12:22
-	1	pSCAT	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/19 17:34
-	10	barlow and ataxia adj telangiectasia	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/19 17:52
-	50	ataxia adj telangiectasia adj gene	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/19 17:54
-	35	(ataxia adj telangiectasia adj gene) and (virus or viral or adenovirus or retrovirus)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/19 17:54
-	0	(ataxia adj telangiectasia adj gene) same (virus or viral or adenovirus or retrovirus)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/19 17:55
-	0	ataxia adj telangiectasia adj gene same expression	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/19 17:54
-	67	ATM same (virus or viral or adenovirus or retrovirus)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/19 17:56
-	28	(ATM same (virus or viral or adenovirus or retrovirus)) and tumor	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/19 17:56
-	2	ATM adj expression	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/19 17:56
-	67	ATM same (virus or viral or adenovirus or retrovirus or vaccinia)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/19 17:59
-	43	(ATM same (virus or viral or adenovirus or retrovirus or vaccinia)) and (express or expression or produce or production)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/19 17:58
-	32181	ATM and (express or expression or produce or production)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/19 17:59
-	5042	ATM same(express or expression or produce or production	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/19 18:03

-	134	(ATM same(express or expression or produce or production)) and (virus or viral or adenovirus or retrovirus or vaccinia)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/19 17:59
-	72	(ATM same(express or expression or produce or production)) and (adenovirus or retrovirus or vaccinia)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/19 17:59
-	53	((ATM same(express or expression or produce or production)) and (adenovirus or retrovirus or vaccinia)) and kinase	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/19 18:00
-	13	(((ATM same(express or expression or produce or production)) and (adenovirus or retrovirus or vaccinia)) and kinase) and (DNA adj repair)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/19 18:01
-	3	ATM adj kinase same (express or expression or produce or production)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/19 18:03
-	2	(ATM adj kinase same (express or expression or produce or production)) and virus	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/12/19 18:03

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NEWS 14 Apr 21    New current awareness alert (SDI) frequency in
                  WPIDS,WPINDEX,WPIX
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                  added to IFIPAT
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NEWS 19 May 19    Simultaneous left and right truncation added to WSCA
NEWS 20 May 19    PATDPA enhanced with new search field, simultaneous left and
                  right truncation
NEWS 21 Jun 09    Simultaneous left and right truncation added to CBNB
NEWS 22 Jun 09    PATDPAFAM enhanced with additional data
NEWS 23 Jun 23    2004 edition of the FSTA Thesaurus is now available
NEWS 24 Jun 28    HSDB has been reloaded
NEWS 25 Jul 16    Data from 1961-1976 added to RUSSIAPAT
NEWS 26 Jul 21    Identification of STN records implemented
NEWS 27 Jul 21    Polymer class term count added to REGISTRY
NEWS 28 Jul 22    INPADOCDB: Basic Index (/BI) enhanced; Simultaneous Left and
                  Right Truncation available

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              MACINTOSH VERSION IS V6.0b ENG AND V6.0Ub(JP), AND
              CURRENT DISCOVER FILE IS DATED 01 APRIL 2004
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                                    ENTRY  SESSION
FULL ESTIMATED COST                 0.21   0.21
The previous command was not recognized by the system.
For a list of commands available to you in the current file, enter
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=> s ATH  A  deficient  A  well
THIS COMMAND IS NOT AVAILABLE IN THE CURRENT FILE
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[illegible] may [illegible] default [illegible]. For example, the PubMed
[illegible] may be used to [illegible] the index to a file which has an
index. Enter "HELP INDEXES" at any Main Menu [illegible] to learn about
[illegible] which can be used in this file.

[illegible]

[illegible]

File ENTREZ.HLP created at [illegible] on [illegible]

File MEDLINE.HLP created at [illegible] on [illegible]

File TAXIDX.HLP created at [illegible] on [illegible]
[illegible] of [illegible] [illegible] [illegible] [illegible] [illegible] [illegible].
File [illegible] "HELP TAXONOMY" for details.
[illegible] [illegible] [illegible] [illegible] [illegible]

[illegible] ATM [illegible] [illegible]
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[illegible]
[illegible] [illegible] [illegible]

[illegible]
[illegible] [illegible] [illegible]

1: Nucleic Acids Res 2002 Dec 15;30(24):5485-96

Accession Number: 12490717
PMID: 12490717
Title: Ataxia telangiectasia-mutated protein kinase activity and
activation depends on the Mre11/Rad50/Nbs1 complex.
Author(s): Lee JH; Paull TT; Department of Molecular Genetics and
Microbiology, University of Texas at Austin, 1 University Station,
Austin, TX 78712, USA.
Source: Nucleic Acids Research 2002 Dec 15;30(24):5485-96
Publication Type: Journal Article; Research Support, U.S. Gov't, P.H.S.
Language: English
Entry Mode: MEDLINE
Entry Date: Entered STN: 20021217
Last Updated on STN: 20030124
Revised Medline: 20030124
Abstract: The ATM protein kinase is activated in response to DNA damage. However, it is unclear how ATM is activated. Mre11 complex (Mre11/Rad50/Nbs1) is required for ATM activation in response to ionizing radiation (IR)-induced DNA damage in vivo. Here, we show that ionizing radiation, IR-mimetic DNA damage and Mre11 complex overexpression all stimulate ATM kinase activity in vitro. Mre11 complex is required for ATM activation in response to IR, but not for activation by DNA damage mimetics. Mre11 complex is also required for ATM activation in Nbs1-deficient cells. Finally, we show that ATM interacts with and phosphorylates Nbs1 in vitro. These results suggest that ATM activation in response to IR may be a critical function of the Mre11 complex in DNA damage signaling.

2: Nucleic Acids Res 2002 Nov 15;30(22):4963-74

Accession Number: 12432014
PMID: 12432014
Title: Regulation of the IRF-1 tumor suppressor gene by the Ataxia
telangiectasia-mutated and AT and Rad3-related DNA damage response
pathways.
Author(s): Kirchhoff JR; Gamper AM; Collis SJ; DeWeese TL; Abler AS;
Tyler DS; Duke Institute of Genome Sciences and Policy, Durham, NC
27710, USA.
Source: Nucleic Acids Research 2002 Nov 15;30(22):4963-74
Publication Type: Journal Article; Research Support, U.S. Gov't, P.H.S.
Language: English
Entry Mode: MEDLINE

ENTRY MONTH: [illegible]
ENTRY DATE: Entered STN: [illegible]
Last Updated on STN: [illegible]
Entered Medline: [illegible]

AB [illegible] by which [illegible] (IRF-1) and the [illegible] DNA damage [illegible]. We demonstrate that IRF-1 and the [illegible] suppressor protein p53 are [illegible] up-regulated during the response to DNA damage in an ATM dependent manner. [illegible] IRF-1 protein by either [illegible] expression and an [illegible] increase in the half life of the IRF-1 protein. A [illegible] in the [illegible] IRF-1 mRNA and IRF-1 protein was [illegible] in ATM **deficient cells**. [illegible] ATM **deficient cells** failed to [illegible] IRF-1 in response to [illegible], the [illegible] IRF-1 in response to [illegible] remained intact. Re-expression of the ATM kinase in AT cells [illegible] the DNA damage [illegible] of IRF-1, whilst the [illegible] kinase inhibitor wortmannin [illegible] IRF-1 [illegible] by DNA damage in ATM positive cells. The data highlight a role for the ATM kinase in [illegible] the [illegible] and transcriptional cooperation of IRF-1 and p53 to regulate p21 expression. Thus, IRF-1 is [illegible] by two distinct signalling pathways; a JAK-STAT signalling pathway in viral infected cells and an ATM signalling pathway in DNA damaged cells.

L4 ANSWER [illegible] MEDLINE [illegible]
ACCESSION NUMBER: [illegible] MEDLINE
DOCUMENT NUMBER: [illegible] PubMed ID: [illegible]
TITLE: ATM is activated in response to N-methyl-N'-nitro-N-nitrosoguanidine-induced DNA alkylation.
AUTHOR: [illegible]
CORPORATE SOURCE: Department of [illegible] Chemistry and Molecular Biology and the Stanley S. [illegible] Cancer Center, [illegible] State University Health Sciences Center, New Orleans, [illegible], USA.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2002 Oct 11) [illegible]
Journal code: [illegible]. ISSN: [illegible].
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: [illegible]
ENTRY DATE: Entered STN: [illegible]
Last Updated on STN: [illegible]
Entered Medline: [illegible]

AB p53 plays an important role in response to ionizing radiation by regulating cell cycle progression and triggering apoptosis. These activities are controlled, in part, by the phosphorylation of p53 by the protein kinase ATM. Recent evidence indicates that the monofunctional DNA alkylating agent N-methyl-N'-nitro-N-nitrosoguanidine (MNNG) also triggers up-regulation and phosphorylation of p53; however, the mechanisms responsible for this are unknown. We observed that in MNNG-treated normal human fibroblasts, up-regulation and phosphorylation of p53 was sensitive to the ATM kinase inhibitor wortmannin. ATM-deficient fibroblasts exhibited a delay in p53 up-regulation, indicating a role for ATM in triggering the MNNG-induced response. Likewise, a mismatch repair (MMR)-deficient colorectal tumor line failed to show rapid up-regulation of p53. However, unlike ATM **deficient cells**, these MMR-deficient cells displayed rapid phosphorylation of the p53 residue serine 15 after MNNG. In vitro kinase assays indicate that ATM is rapidly activated in both normal and MMR-deficient cells in response to MNNG. Using a number of morphological and biochemical approaches, we failed to observe MNNG-induced apoptosis in normal human fibroblasts, suggesting that apoptosis-induced DNA strand breaks are not required for the activation of ATM in response to MNNG. [illegible] assays indicated that strand breaks accumulated, and p53 [illegible] phosphorylation occurred quite rapidly (within [illegible] min) after MNNG treatment, suggesting that DNA strand breaks that arise during the repair process activate ATM. These findings indicate that ATM activation is not limited to the ionizing radiation-induced response and potentially plays an important role in response to DNA alkylation.

L4 ANSWER [illegible] MEDLINE [illegible]
ACCESSION NUMBER: [illegible] MEDLINE
DOCUMENT NUMBER: [illegible] PubMed ID: [illegible]
TITLE: DNA-PK and ATM are required for [illegible]-enhanced integration.
AUTHOR: [illegible]

AUTHOR(S): Department of Experimental Radiation Oncology, The University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, TX 77030, USA.
NLM UNIQUE ID: 9417353
MEDLINE STATUS: MEDLINE
SOURCE: RADIATION RESEARCH, (2002 May) 157 (5) 525-35.
Journal code: 0401245. ISSN: 0033-7587.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200207
ENTRY DATE: Entered STN: 20020722
Last Updated on STN: 20030117
Entered Medline: 20020621
AB Ionizing radiation (IR) is known to activate multiple cell cycle checkpoints that are thought to enhance the ability of cells to repair DNA damage. Protein phosphatase 2A (PP2A) has been implicated in IR-induced activation of these checkpoints; therefore, human cells were exposed to various doses of IR in order to determine the effect of IR on PP2A activity. PP2A was extracted from cells and analyzed for PP2A by Mono Q anion exchange chromatography and microcystin affinity chromatography. PP2A exists in cells in two forms, as a heterodimer consisting of a 65-kDa scaffolding subunit (A) plus a 36 kDa catalytic subunit (C), and as ABC heterotrimers, containing one of a variety of regulatory (B) subunits. Here we show that IR promotes a transient and reversible reduction in the amount of nuclear AB(1) heterotrimer without affecting the AB(2) heterotrimer or AC heterodimer. In stably radiation-resistant, **ATM deficient** cells the amount of nuclear PP2A heterotrimer returned to control levels, but the reduction was not restored by radiation, in the radiation-sensitive wild-type ATM. Furthermore, in these cells with plasmid-encoded ATM, wild-type but not kinase-inactive ATM promoted the IR-induced reduction in nuclear PP2A heterotrimer. The changes in nuclear PP2A occurred without a significant difference in the overall cellular content of the A, B, or C subunits, which remained confined to the nucleus. We conclude that ATM deficient cells regulate but do not respond to IR by altering nuclear PP2A.

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Department of Radiation Oncology, The University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, TX 77030, USA.
NLM UNIQUE ID: 9502503
MEDLINE STATUS: MEDLINE
PUBMED ID: 11724140
TITLE: ATM dependent activation of BRF1 regulates DNA damage and cell fate in human breast cancer cells in response to ionizing radiation.
AUTHOR: Sun Chang Y; Brattain Michael G; Zhang James M
AUTHOR(S): Department of Radiation Oncology, University of Virginia Health Science System, Charlottesville, Virginia 22908, USA.
NLM UNIQUE ID: 9422822 (JOURNAL ARTICLE)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2002 Feb 15) 277 (7) 4949-56.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 20020227
Last Updated on STN: 20030117
Entered Medline: 20020321
AB Ionizing radiation (IR) is known to activate multiple cell cycle checkpoints that are thought to enhance the ability of cells to repair DNA damage. Protein phosphatase 2A (PP2A) has been implicated in IR-induced activation of these checkpoints; therefore, human cells were exposed to various doses of IR in order to determine the effect of IR on PP2A activity. PP2A was extracted from cells and analyzed for PP2A by Mono Q anion exchange chromatography and microcystin affinity chromatography. PP2A exists in cells in two forms, as a heterodimer consisting of a 65-kDa scaffolding subunit (A) plus a 36 kDa catalytic subunit (C), and as ABC heterotrimers, containing one of a variety of regulatory (B) subunits. Here we show that IR promotes a transient and reversible reduction in the amount of nuclear AB(1) heterotrimer without affecting the AB(2) heterotrimer or AC heterodimer. In stably radiation-resistant, **ATM deficient** cells the amount of nuclear PP2A heterotrimer returned to control levels, but the reduction was not restored by radiation, in the radiation-sensitive wild-type ATM. Furthermore, in these cells with plasmid-encoded ATM, wild-type but not kinase-inactive ATM promoted the IR-induced reduction in nuclear PP2A heterotrimer. The changes in nuclear PP2A occurred without a significant difference in the overall cellular content of the A, B, or C subunits, which remained confined to the nucleus. We conclude that ATM deficient cells regulate but do not respond to IR by altering nuclear PP2A.

response to IR.

L4 ANSWER [illegible] OF 19 MEDLINE on STN
ACCESSION NUMBER: [illegible] MEDLINE
DOCUMENT NUMBER: [illegible] PubMed ID: [illegible]
TITLE: ATM-dependent phosphorylation of human Rad9 is required for ionizing radiation-induced checkpoint activation.
AUTHOR: Chen M J; Lin Y T; Lieberman H B; Chen G; Lee E Y
CORPORATE SOURCE: Department of Molecular Medicine/Institute of Biotechnology, The University of Texas Health Science Center, San Antonio, Texas [illegible], USA.
CONTRACT NUMBER: [illegible]
[illegible]
[illegible]
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, **(2001 May 11)** [illegible].
Journal code: [illegible]. ISSN: [illegible].
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: [illegible]
ENTRY DATE: Entered STN: [illegible]
Last Updated on STN: [illegible]
Entered Medline: [illegible]

AB ATM (ataxia telangiectasia mutated) is a Ser/Thr kinase involved in cell cycle checkpoints and DNA repair. Human Rad9 (hRad9) is the homologue of Schizosaccharomyces pombe Rad9 protein that plays a critical role in cell cycle checkpoint control. To examine the potential signaling pathway linking ATM and hRad9, we investigated the modification of hRad9 in response to DNA damage. Here we show that hRad9 protein is constitutively phosphorylated in undamaged cells and undergoes hyperphosphorylation upon treatment with ionizing radiation (IR), ultraviolet light (UV), and hydroxyurea (HU). Interestingly, hyperphosphorylation of hRad9 induced by IR is dependent on ATM. Ser 272 of hRad9 is phosphorylated directly by ATM in vitro. Furthermore, hRad9 is phosphorylated on Ser 272 in response to IR in vivo, and this modification is delayed in **ATM deficient cells**. Expression of hRad9 S272A mutant protein in human lung fibroblast VA13 cells disturbs IR-induced G1/S checkpoint activation and increased cellular sensitivity to IR. Together, our results suggest that the ATM-mediated phosphorylation of hRad9 is required for IR-induced checkpoint activation.

L4 ANSWER [illegible] OF 19 MEDLINE on STN
ACCESSION NUMBER: [illegible] MEDLINE
DOCUMENT NUMBER: [illegible] PubMed ID: [illegible]
TITLE: Tumor suppressor p53 binding protein 1 (53BP1) is involved in DNA damage-signaling pathways.
COMMENT: Erratum in: J Cell Biol. 2001 Jul [illegible]
AUTHOR: Rappold I; Iwabuchi K; Date T; Chen J
CORPORATE SOURCE: Division of Oncology Research, Mayo Clinic, Rochester, Minnesota [illegible], USA.
SOURCE: JOURNAL OF CELL BIOLOGY, **(2001 Apr 30)** [illegible] [illegible]-21.
Journal code: [illegible]. ISSN: [illegible].
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: [illegible]
ENTRY DATE: Entered STN: [illegible]
Last Updated on STN: [illegible]
Entered Medline: [illegible]

AB The tumor suppressor p53 binding protein 1 (53BP1) binds to the DNA-binding domain of p53 and enhances p53-mediated transcriptional activation. 53BP1 contains two breast cancer susceptibility gene 1 C terminus (BRCT) motifs, which are present in several proteins involved in DNA repair and/or DNA damage-signaling pathways. Thus, we investigated the potential role of 53BP1 in DNA damage-signaling pathways. Here, we report that 53BP1 becomes hyperphosphorylated and forms discrete nuclear foci in response to DNA damage. These foci colocalize at all time points with phosphorylated H2AX (gamma-H2AX), which has been previously demonstrated to localize at sites of DNA strand breaks. 53BP1 foci formation is not restricted to gamma radiation but is also detected in response to UV radiation as well as hydroxyurea, camptothecin, etoposide, and methylmethanesulfonate treatment. Several observations suggest that 53BP1 is regulated by ataxia telangiectasia mutated (ATM) after DNA damage. First, **ATM deficient cells** show no 53BP1 hyperphosphorylation and reduced 53BP1 foci formation in response to gamma radiation compared with cells expressing wild-type ATM. Second,

w[illegible] treatment [illegible] [illegible] [illegible] [illegible] hyperphosphorylation and [illegible] formation [illegible] [illegible]. Third, [illegible] is readily phosphorylated by ATM in vitro. Taken together, these results suggest that [illegible] is an ATM substrate that is involved early in the DNA damage signaling pathway in mammalian cells.

L4 ANSWER 4 OF 15 MEDLINE on STN
ACCESSION NUMBER: [illegible] MEDLINE
DOCUMENT NUMBER: [illegible] PubMed ID: [illegible]
TITLE: The plant isoflavenoid genistein activates p53 and Chk2 in an ATM-dependent manner.
AUTHOR: Ye R; [illegible]; [illegible]; [illegible]; [illegible]; Lees-Miller S P
CORPORATE SOURCE: Department of Biochemical Sciences, University of Calgary, Calgary, Alberta T2N 4N1, Canada.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 Feb 16) 276 (7) 4828-33.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: [illegible]
ENTRY DATE: Entered STN: [illegible]
Last Updated on STN: [illegible]
Entered Medline: [illegible]

AB Genistein is an isoflavenoid that is abundant in soy beans. Genistein has been reported to have a wide range of biological activities and to play a role in the diminished incidence of breast cancer in populations that consume a soy rich diet. Genistein was originally identified as an inhibitor of tyrosine kinases; however, it also inhibits topoisomerase II by stabilizing the covalent DNA cleavage complex, an event predicted to cause DNA damage. The topoisomerase II inhibitor etoposide acts in a similar manner. Here we show that genistein induces the up-regulation of p53 protein, phosphorylation of p53 at serine 15, activation of the sequence-specific DNA binding properties of p53, and phosphorylation of the [illegible] Chk2 protein kinase at threonine 68. Phosphorylation and activation of p53 and phosphorylation of Chk2 were not observed in **ATM deficient cells**. In contrast, the topoisomerase II inhibitor etoposide induced phosphorylation of p53 and Chk2 in ATM-positive and **ATM deficient cells**. In addition, genistein treated **ATM deficient cells** were significantly more susceptible to genistein-induced killing than were ATM positive cells. Together our data suggest that ATM is required for activation of a DNA damage-induced pathway that activates p53 and Chk2 in response to genistein.

L4 ANSWER 5 OF 15 MEDLINE on STN
ACCESSION NUMBER: [illegible] MEDLINE
DOCUMENT NUMBER: [illegible] PubMed ID: [illegible]
TITLE: Synthetic lethality between mutation in Atm and DNA-PK(cs) during murine embryogenesis.
AUTHOR: Gurley K E; Kemp C J
CORPORATE SOURCE: Fred Hutchinson Cancer Research Center [illegible], 1100 Fairview Ave. N., Seattle, WA 98109-1024, USA.
SOURCE: CURRENT BIOLOGY, (2001 Feb 6) 11 (3) 191-4.
Journal code: 9107782. ISSN: 0960-9822.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: [illegible]
ENTRY DATE: Entered STN: [illegible]
Last Updated on STN: [illegible]
Entered Medline: [illegible]

AB The gene product mutated in ataxia telangiectasia, ATM, is a ubiquitously expressed [illegible] kDa protein kinase that is a key mediator of the cellular response to DNA damage [1]. **ATM deficient cells** are radiosensitive and show impaired cell cycle arrest and increased chromosome breaks in response to ionizing radiation. ATM is a member of the phosphatidylinositol 3-kinase (PI3K)-related protein kinase superfamily, which includes the catalytic subunit of DNA-dependent protein kinase (DNA-PKcs) and ATR [2]. DNA-PK is a [illegible] kDa protein kinase that is required for proper end-to-end rejoining of DNA double strand breaks [3]. [illegible] mice have a [illegible] mutation in the gene encoding DNA-PKcs and, like Atm[illegible] mice, are viable and radiosensitive [4-6]. To determine if Atm and DNA-PKcs show genetic interaction, we attempted to generate mice deficient in both gene products. However, no [illegible] Atm[illegible] pups were recovered from [illegible] Atm[illegible] intercrosses. Developmental arrest of [illegible] Atm[illegible] embryos occurred

at cell [illegible] a novel potential stage where entry into [illegible] are hypersensitive to DNA damage [illegible]. These novel synthetic lethality between [illegible] ATM and DNA-PK and suggest that ATM and DNA-PK have complementary functions that are essential for normal growth.

L4 ANSWER 11 OF 19 MEDLINE on STN
ACCESSION NUMBER: [illegible] MEDLINE
DOCUMENT NUMBER: [illegible] PubMed ID: [illegible]
TITLE: Partial differentiation blocks premature mitotic entry and centrosome overduplication.
AUTHOR: [illegible]; Mailhes J B; Fuseler J W; Boivin G P; Young D
CORPORATE SOURCE: Medical Research Laboratory, Department of Medicine, and Department of Pharmacology, University of Maryland, School of Medicine, Baltimore, Maryland [illegible], USA.
SOURCE: [illegible]
[illegible]
PUB. TYPE: Journal; Article; JOURNAL ARTICLE
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; JOURNAL ARTICLE
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: [illegible]
ENTRY DATE: Entered STN: [illegible]
Last Updated on STN: [illegible]
Entered Medline: [illegible]
AB We previously reported that overexpression of protein kinase C [illegible] in HeLa cells arrest, and that the p34 CDC2 kinase associated cell cycle arrest [illegible] with type BPA. These findings prompted us to investigate if the [illegible] mutations which increase cell cycle arrest [illegible] with type BPA when overexpressed in either HeLa cells [illegible] an ATM deficient cell line. We detected a subtle difference in the degree to which these BPA mutants induce arrest. BPA [illegible] retained their ability to [illegible] the most [illegible] with the BPA [illegible], with the BPA [illegible] mutant [illegible] the least [illegible] to [illegible], compared to wild type BPA. The degree to which the different mutants [illegible] cell cycle progression correlated somewhat with the age of AI tumor cultured by the [illegible] carriers. [illegible] analysis of protein extracts from [illegible] overexpressing cells indicated that the cell cycle regulated cytoplasmic pool of beta-catenin is dramatically reduced, whereas the insoluble nonchromatin pool remains essentially unaffected. We discuss the implications of these findings in relation to cell cycle arrest, apoptosis and AD.

L4 ANSWER 12 OF 19 MEDLINE on STN
ACCESSION NUMBER: [illegible] MEDLINE
DOCUMENT NUMBER: [illegible] PubMed ID: [illegible]
TITLE Regulation of DNA-dependent protein kinase activity by [illegible] radiation activated Akt kinase in an ATM-dependent pathway.
AUTHOR: Chunduru S; Brown K D; Allalunis-Turner M J; Pinkerton J; Ng B; Pandita T K; Hosoya N; Taucher-Scholz G; Kamiya K; Bedford J; Morgan W F; Kaufman D G; Gupta S
CORPORATE SOURCE: Department of Molecular Genetics and Biochemistry and the Department of Pharmacology, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania [illegible], USA.
SOURCE: [illegible]
[illegible]
PUB. TYPE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Sep 29)
[illegible]
Journal code: [illegible]. ISSN: [illegible].
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; JOURNAL ARTICLE
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: [illegible]
ENTRY DATE: Entered STN: [illegible]
Last Updated on STN: [illegible]
Entered Medline: [illegible]
AB [illegible] ionizing radiation (IR) treatment results in activation of the autophosphorylation of the DNA dependent protein kinase (DNA-PK) catalytic subunit (DNA-PKcs) and thus potentially activates Akt kinase activity in resistant cells. To understand the role of ATM and DNA-PK in the activation of Akt, we analyzed Akt, ATM, and DNA-PK activity in ATM- and DNA-PK-deficient cells after irradiation. Our results show that despite the presence of higher than normal levels of DNA-PK kinase activity, no Akt activation was detected after IR exposure in ATM deficient cells. Conversely, normal activation of Akt in ATM- and Akt-mutant or DNA-PK-deficient cells, indicating that ATM and

[illegible] DNA-PK is required for activation of ATM in response to IR treatment. However, activation of ATM kinase activity by IR irradiated cells with activation of ATM activity in all phases of the cell cycle. These results suggest that ATM is primarily responsible for activation of ATM in response to IR throughout the cell cycle independent from DNA-PK activity. In addition, the requirement of DNA-PK for activation of ATM in response to IR through ATM kinase activity. Collectively, these results suggest a [illegible] interdependence of the ATM and DNA-PK pathways in the cellular response to IR through ATM kinase.

L4 ANSWER 12 OF 19 MEDLINE on STN
ACCESSION NUMBER: 2000[illegible] MEDLINE
DOCUMENT NUMBER: 20[illegible] PubMed ID: [illegible]
TITLE: Ionizing radiation induces ATM kinase activation by, Wortmannin, [illegible] DNA-PK, and, independent activation of p21 protein after gamma irradiation, [illegible] the presence.
AUTHOR: Kim S.H.; Wu M.L.; Lee S.H.; Kim T.H.; Park J.
CORPORATE AUTHOR: Department of Microbiology, Chonnam University, Kwangju, [illegible] Republic of Korea.
SOURCE: [illegible] MOLECULAR BIOLOGY, (2000 Apr 17) 142[illegible] [illegible].
Journal code: [illegible]. ISSN: 0006-[illegible].
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: [illegible]
ENTRY DATE: Entered STN: 20 [illegible]
Last Updated on STN: 20 [illegible]
Entered Medline: 2000[illegible]
AB [illegible] [illegible] the cellular kinase activity, p21, in [illegible] irradiated cells, [illegible] by the activation pathway. Recently, we reported that DNA damage is required for efficient p21 expression by demonstrating that enhanced p21 mRNA expression induced by DNA damage results in increased p21 protein, but enhanced p21 mRNA without DNA damage does not. In addition, we demonstrated that DNA damage increased the stabilization of p21. In this study, we analyze the link between p21 stabilization and DNA damage. Enhanced p21 protein expression in ML-1 cells resulting from IR, gamma irradiation was diminished by Wortmannin or LY294002 pretreatment of cells. However, the levels of p21 mRNA were not affected by inhibitor pretreatment. Wortmannin or LY294002 pretreatment reduces p21 expression after gamma-irradiation to a lesser degree than that of p21. In addition, we examined the involvement of DNA-PK, whose activity is inhibited by Wortmannin or LY294002, in p21 stabilization using the SCID fibroblast cell line and a DNA-PK targeting ML-1 cell line. Accumulation of p21 protein by gamma irradiation was similar to that in DNA-PK intact cells and was reduced by Wortmannin or LY294002 pretreatment. Involvement of another DNA damage detecting enzyme, the ATM gene product, whose activity is also inhibited by Wortmannin or LY294002, was evaluated. ATM deficient cells showed p21 after gamma irradiation, gamma irradiation-induced p21 protein was diminished by pretreatment of cells with Wortmannin or LY294002. We conclude that the p21 stabilization mechanism functions after gamma irradiation, was sensitive to Wortmannin or LY294002, and required neither DNA-PK nor ATM gene product for activity.

L4 ANSWER 14 OF 19 MEDLINE on STN
ACCESSION NUMBER: 2[illegible] MEDLINE
DOCUMENT NUMBER: 2[illegible] PubMed ID: [illegible]
TITLE: ATM: a mediator of multiple responses to genotoxic stress.
AUTHOR: Rotman G.; Shiloh Y.
CORPORATE AUTHOR: Department of Human Genetics and Molecular Medicine, Sackler School of Medicine, Tel Aviv University, Ramat Aviv 69978, Israel.
SOURCE: [illegible] (1999 Nov 1) 14 4[illegible] 414-44. Ref: [illegible]
Journal code: [illegible]. ISSN: 0891-[illegible].
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; REVIEW
(REVIEW, TUT Pilot
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: [illegible]
ENTRY DATE: Entered STN: 21 [illegible]
Last Updated on STN: 20 [illegible]
Entered Medline: [illegible]
AB The ATM protein kinase is the product of the gene responsible for the

[illegible] **ATM deficient cells** [illegible]

L4 ANSWER 14 OF 19 MEDLINE on STN
ACCESSION NUMBER: [illegible] MEDLINE
DOCUMENT NUMBER: [illegible] PubMed ID: [illegible]
TITLE: [illegible]
AUTHOR: [illegible]
CORPORATE SOURCE: [illegible]
SOURCE: [illegible]
PUB. TYPE: [illegible]
DOCUMENT TYPE: [illegible]
LANGUAGE: [illegible]
FILE SEGMENT: [illegible]
ENTRY MONTH: [illegible]
ENTRY DATE: [illegible]
AB [illegible]

L4 ANSWER 15 OF 19 MEDLINE on STN
ACCESSION NUMBER: [illegible] MEDLINE
DOCUMENT NUMBER: [illegible] PubMed ID: [illegible]
TITLE: [illegible]
AUTHOR: [illegible]
CORPORATE SOURCE: [illegible]
SOURCE: [illegible]
PUB. TYPE: [illegible]
DOCUMENT TYPE: [illegible]
LANGUAGE: [illegible]
FILE SEGMENT: [illegible]
ENTRY MONTH: [illegible]
ENTRY DATE: [illegible]
AB [illegible]

with the kinetics of multiple DNA damage-induced cell cycle checkpoints. The mutability of these checkpoints defects in ataxia-telangiectasia (A-T) cells has suggested that wortmannin may inhibit one or more ATM-dependent checkpoint pathways in DNA-treated cells. We now show that wortmannin inhibits the catalytic activity of both ATM and the related kinase, ATM and Rad3-related (ATR), at concentrations similar to those that cause radiosensitization. Moreover, like ATM deficient cells, wortmannin-treated A-T lymphoblastoid cells exhibit premature chromosome condensation, similar to irradiated cells exhibit radioresistant DNA synthesis. Similar to ataxia-telangiectasia cells, wortmannin-treated cells exhibit defective S and G2 checkpoint control following exposure to ionizing radiation. These results suggest that the ATM and ATR kinases, DNA-dependent protein kinase, another ATM-related protein involved in DNA damage repair, may be important targets affected by wortmannin. Likewise, the radiosensitizing activity of the PI-3 kinase inhibitor, LY294002, was also substantially suppressed by wortmannin-treated cells. These data suggest that the radiosensitizing effects of wortmannin are related to inhibition of the phosphatidylinositol 3-kinase related kinases (PIKKs) and that these proteins are relevant targets for the development of novel antineoplastic agents.

14/ ANSWER 10 OF 19 MEDLINE on STN
ACCESSION NUMBER: 1998414417 MEDLINE
DOCUMENT NUMBER: 98414417 PubMed ID: 9705927
TITLE: Wortmannin, a specific inhibitor of phosphatidylinositol 3-kinase modulates antigen-induced degranulation of human peripheral blood eosinophils.
AUTHOR: Okayama Y; Kawasaki A; Ono S N; Williams F M; Saito H; Ra C
CORPORATE SOURCE: Department of Molecular Pathophysiology, National Institute of Health and Nutrition, Tokyo, Japan.
SOURCE: JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (1998 Aug) 102 (2) 277-86.
Journal code: 1275002. ISSN: 0091-6749.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (CLINICAL TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 19980916
Last Updated on STN: 20020402
Entered Medline: 19981113
AB Members of the phosphatidylinositol 3-kinase related kinase (PIKK) family function in both cell cycle progression and DNA damage-induced cell cycle checkpoints. The fungal metabolite, wortmannin, is an effective radiosensitizer that irreversibly inhibits certain members of the PIKK family. Based on their role in DNA damage responses, several PIKKs, DNA dependent protein kinase (DNA-PK), ataxia telangiectasia mutated (ATM) and the ataxia and Rad3 related protein (ATR), are potential targets for the radiosensitizing effects of wortmannin. In this report, we demonstrate that wortmannin is a relatively potent inhibitor of DNA-PK (IC50, 16 nM) and ATM (IC50, 150 nM) activities, whereas ATR activity is significantly less sensitive to this drug (IC50, 1.8 microM). In intact A549 lung adenocarcinoma cells, wortmannin inhibited both DNA-PK and ATM at concentrations that correlated closely with those required for radiosensitization. Furthermore, pretreatment of A549 cells with wortmannin resulted in radioresistant DNA synthesis, a characteristic abnormality of ATM deficient cells. These results identify wortmannin as an inhibitor of ATM activity and suggest that ATM and DNA-PK are relevant targets for the radiosensitizing effect of this drug in tumor cells.

15/ ANSWER 11 OF 19 MEDLINE on STN
ACCESSION NUMBER: 1998161196 MEDLINE
DOCUMENT NUMBER: 98161196 PubMed ID: 9490649
TITLE: Atm selectively regulates distinct p53-dependent cell-cycle checkpoint and p53-independent pathways.
AUTHOR: Brown K D; Rathmell W K; Wilkerson M D; Bogler O; Waldman T; McMahon M
CORPORATE SOURCE: Department of Molecular Pharmacology and Biological Chemistry, Northwestern University Medical School, Chicago, Illinois 60611, USA.
SOURCE: MOLECULAR AND CELLULAR BIOLOGY, (1997 Dec) 17 (12) 6900-9.
Journal code: 8109063. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (RESEARCH SUPPORT)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199712

[illegible] DATE: Entered [illegible]
Last [illegible] on ATDB: [illegible]
Entered Medline: [illegible]

AB The Atm protein is a protein that belongs to [illegible] family of [illegible] kinases. This pathway includes p53, the **Atm deficient cell** [illegible] and the [illegible] p53 activity after IR. p53 is a nuclear [illegible] that [illegible] cell cycle progression and apoptosis in response to [illegible] DNA damage. However, the mechanism by which p53 is activated downstream of Atm is unknown. To determine the relationship between Atm and p53, we examined cell cycle and apoptotic responses in Atm [illegible] cell lines after IR in the wild-type, Atm heterozygous, and Atm homozygous [illegible] lines were not significantly different from Atm [illegible] cell lines. IR-induced cell cycle checkpoint activation [illegible] was attenuated in thymus from Atm [illegible] mice. However, IR-induced apoptosis was not significantly different in thymocytes from Atm [illegible] mice. These results suggest that Atm is not required for p53 activation in response to IR, but only [illegible] p53-dependent functions. Our results suggest a model in which a [illegible] effect is seen in Atm heterozygous cells [illegible] specific downstream pathway, possibly a mechanism for [illegible] cell cycle and apoptosis responses.

[illegible] AUTHOR [illegible] MEDLINE [illegible]
ACCESSION NUMBER: [illegible] MEDLINE
[illegible] NUMBER: [illegible] PubMed ID: [illegible]
TITLE: The mei-41 gene [illegible] related protein and a [illegible] that [illegible] the human [illegible] gene.
AUTHOR: Hall P.; Laurencon A.; Dekelbaum [illegible]; Martin P.; Green A.; Hawley R.
[illegible] AFFILIATION: Department of Genetics, University of [illegible], Davis 95616, USA.
JOURNAL: Cell, (1995 Sep 8) 82 [illegible] 865-73.
Journal [illegible] Code: [illegible] ISSN: [illegible]
PUB. COUNTRY: United States
[illegible] TYPE: Journal; Article; JOURNAL ARTICLE
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER ABS: GENBANK/U49827
ENTRY MONTH: 199511
ENTRY DATE: Entered STN: 19951109
Last [illegible] on STN: 19951109
Entered Medline: 19951101

AB The Mei-41 serine/threonine kinase is required for DNA repair, mitotic chromosome stability, and normal levels of meiotic recombination in Drosophila. Here we show that the predicted mei-41 protein is similar in sequence to the ATM (ataxia telangiectasia mutated) protein from humans and to the yeast Rad3 and Mec1 proteins. There is also extensive functional overlap between mei-41 and ATM. Like **ATM-deficient cells**, mei-41 cells are exquisitely sensitive to ionizing radiation and display high levels of mitotic chromosome instability. We also demonstrate that mei-41 cells, like **ATM-deficient cells**, fail to show an irradiation-induced delay in the entry into mitosis that is characteristic of normal cells. Thus, the mei-41 gene of Drosophila may be considered to be a functional homolog of the human ATM gene.

[illegible] AUTHOR [illegible] [illegible] COPYRIGHT 2000 ACM, Inc.
ACCESSION NUMBER: [illegible] [illegible] [illegible]
[illegible] NUMBER: [illegible]
TITLE: Atm deficient mice Purkinje cells show age dependent defects in calcium spike bursts and calcium currents
AUTHOR: Inoue, M.; Parker, A.; Wyatt-Burke, A.; Brown, K.; Temple, F.
[illegible] AFFILIATION: Department of Neuroscience, University of Turin, Turin, Italy
JOURNAL: Neuroscience Letters, 2000, [illegible] [illegible] CODEN: NSLED; ISSN: [illegible]
PUBLISHER: Elsevier Science Ltd.
[illegible] TYPE: Journal
LANGUAGE: English

AB Ataxia telangiectasia in humans results in neurodegeneration, immunodeficiency, cancer predisposition and premature aging. Atm knockout mice are viable and exhibit many features of human ataxia telangiectasia patients in the developing, mainly Purkinje cells are affected. We have generated Atm-deficient mice which display neurological abnormalities by several tests. These mice functionally interact with Atm in mediating [illegible] functions, but without [illegible] evidence of neurodegeneration. Here we performed a more detailed morphological and